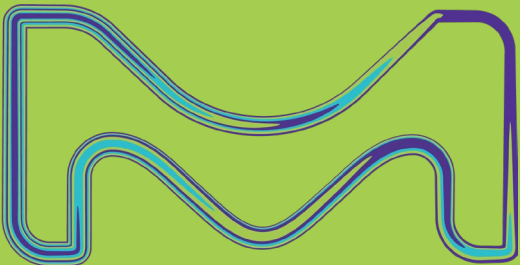


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Disability Accumulation in Multiple sclerosis



10/2024
US-NONNI-01313

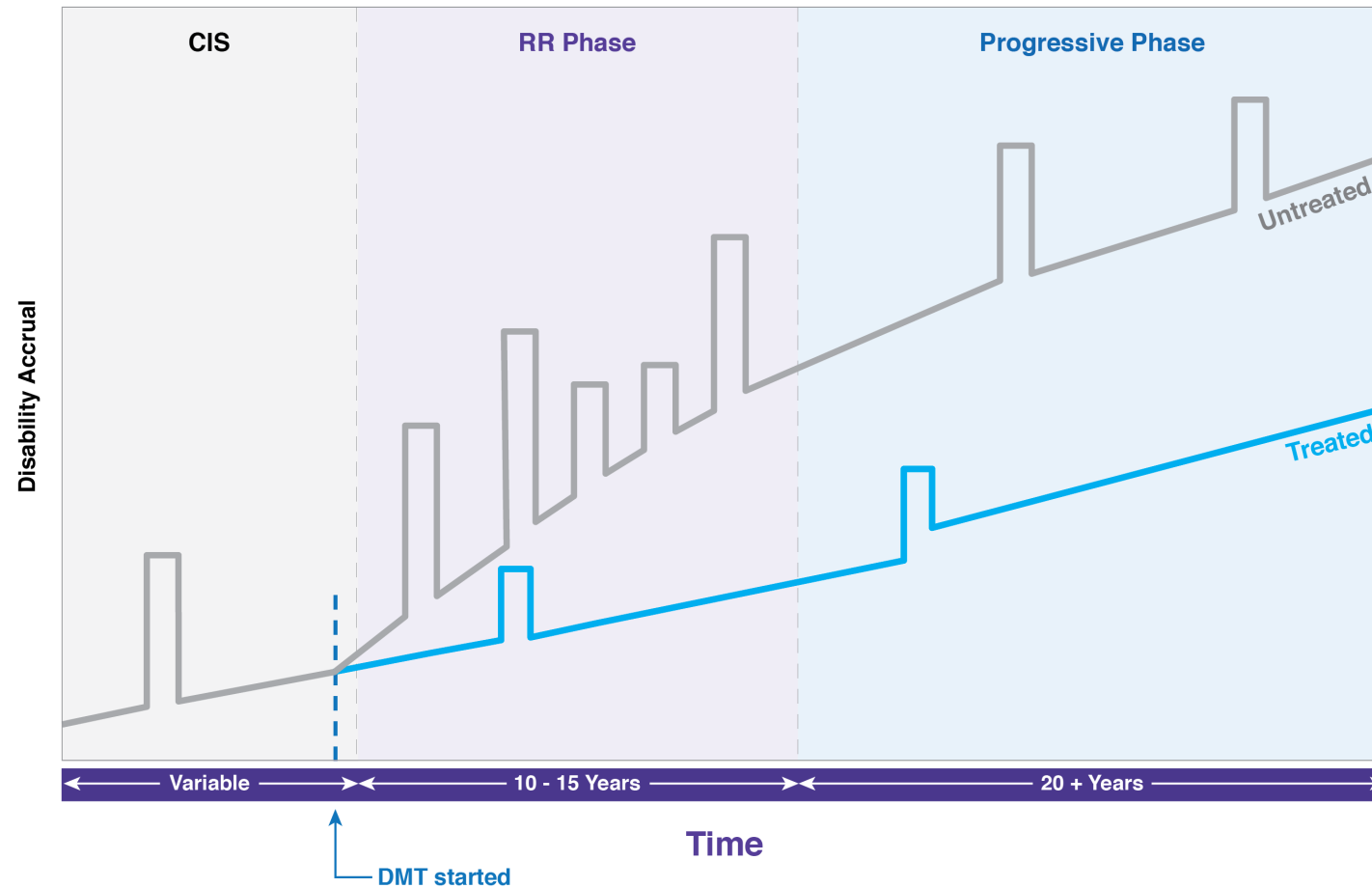
**EMD
SERONO**

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Despite effective relapse reduction with treatment, patients continue to accrue disability

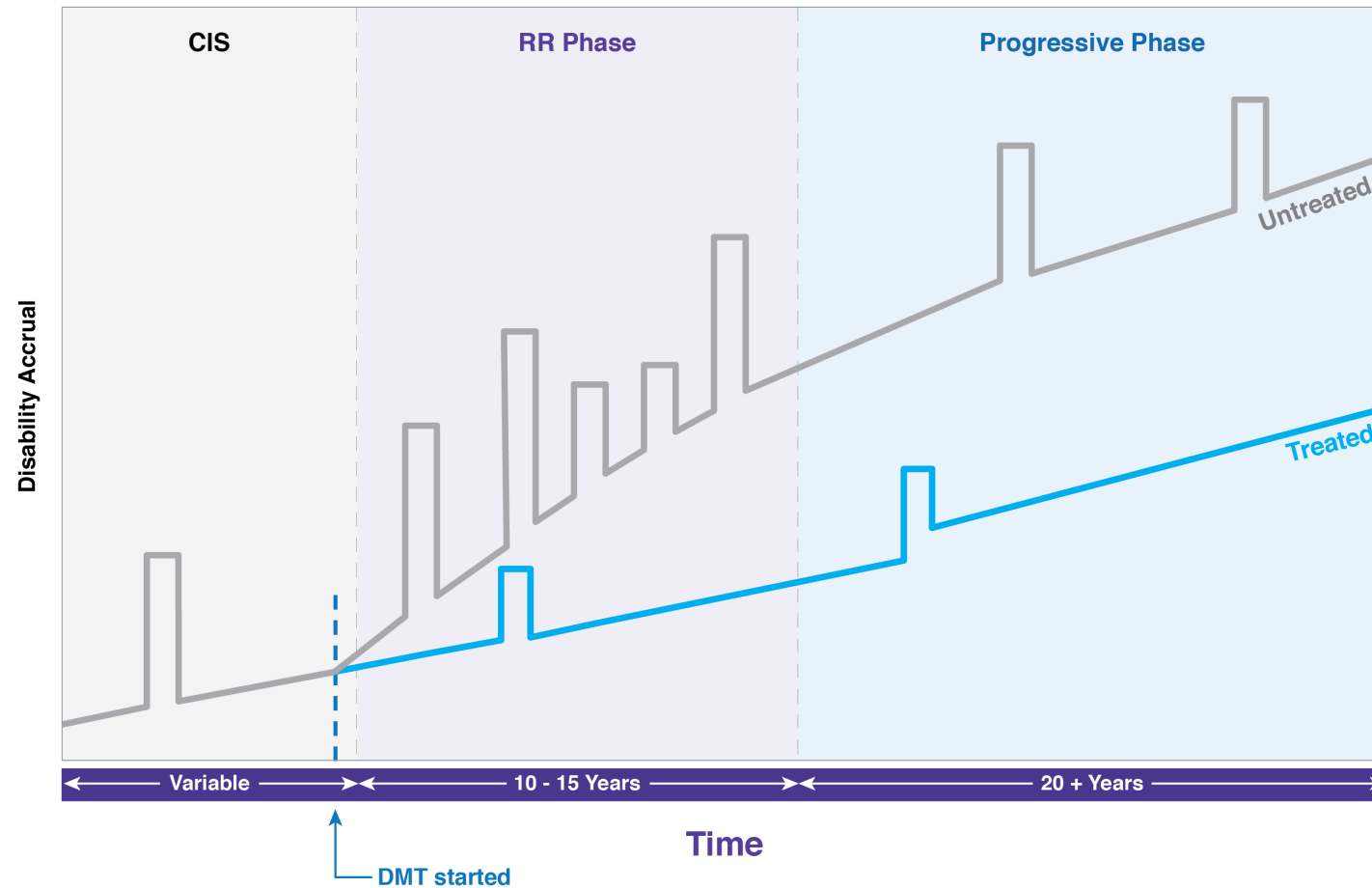


Current MS treatments reduce focal inflammation, relapses, and relapse-associated progression

CIS, clinically isolated syndrome; DMT, disease modifying therapy; MS, multiple sclerosis; RR, relapsing-remitting
The graphic is for illustrative purposes only and not related to the effect of specific therapies



Despite effective relapse reduction with treatment, patients continue to accrue disability



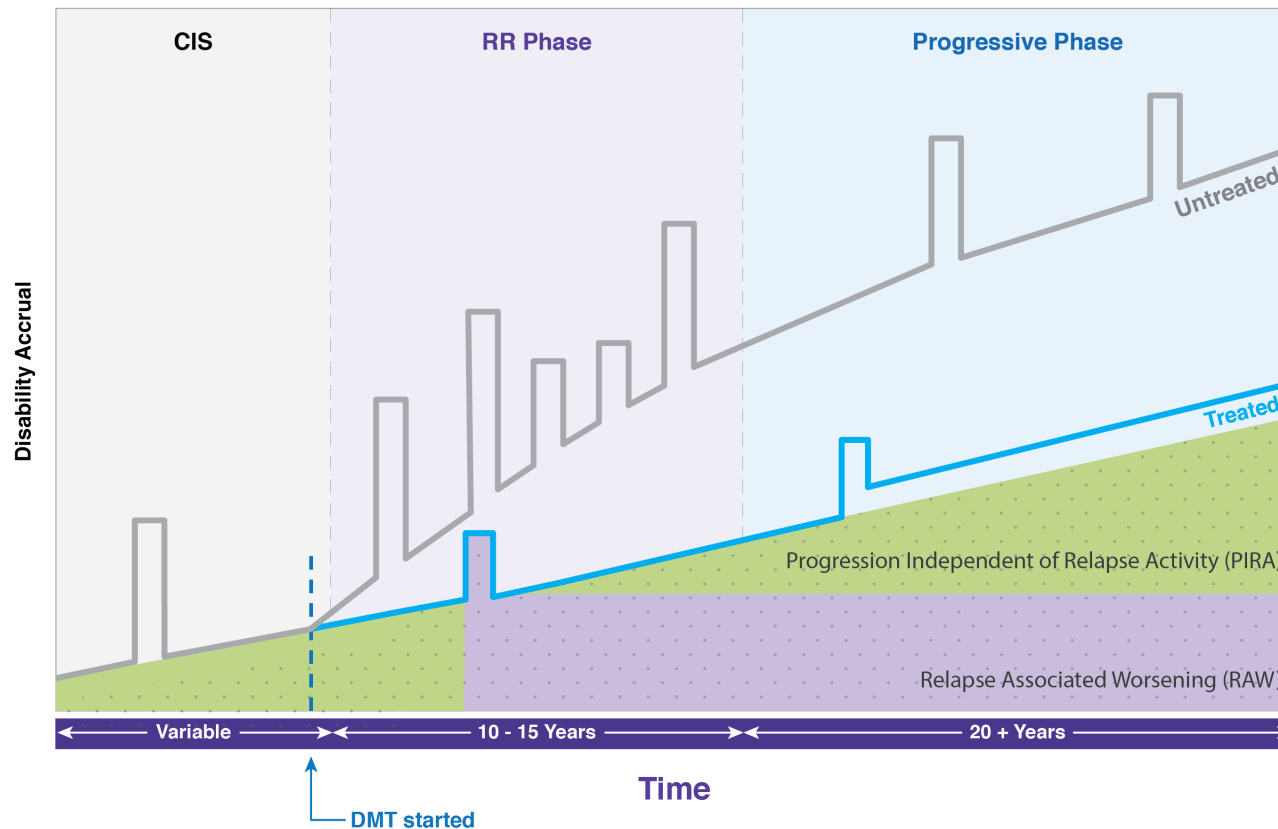
Current MS treatments reduce focal inflammation, relapses, and relapse-associated progression

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Hauser SL, Cree BAC. *Am J Med*. 2020;133(12):1380-1390.



Progression independent of relapse activity occurs from the earliest stages of MS¹



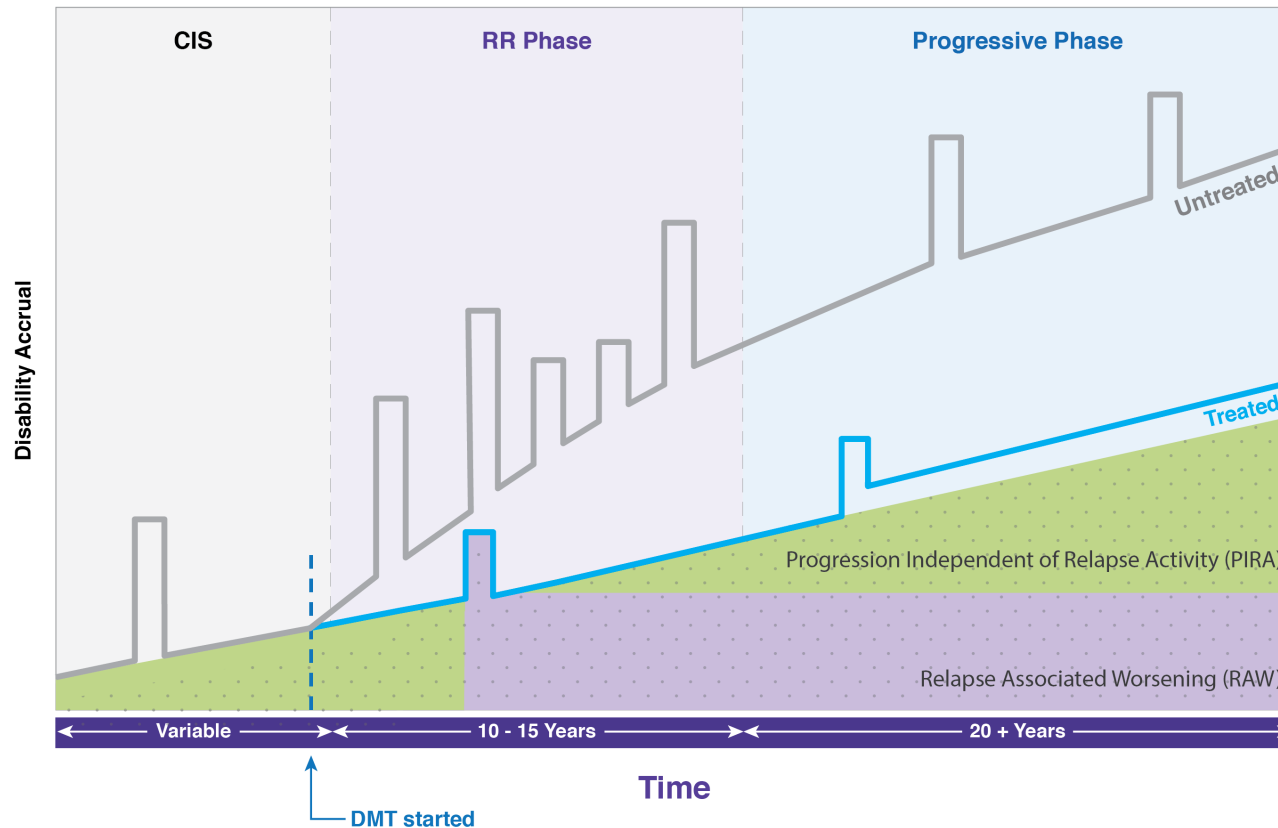
PIRA is a sustained increase in disability that occurs independently of relapse measured after re-baselining following relapse recovery^{2,3}.

RAW is a sustained increase in disability that begins with an incomplete relapse recovery⁴.

CIS, clinically isolated syndrome; DMT, disease modifying therapy; MS, multiple sclerosis; PIRA, progression independent of relapse activity; RAW, relapse-associated worsening; RR, relapsing-remitting
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Progression independent of relapse activity occurs from the earliest stages of MS¹



PIRA is a sustained increase in disability that occurs independently of relapse measured after re-baselining following relapse recovery^{2,3}.

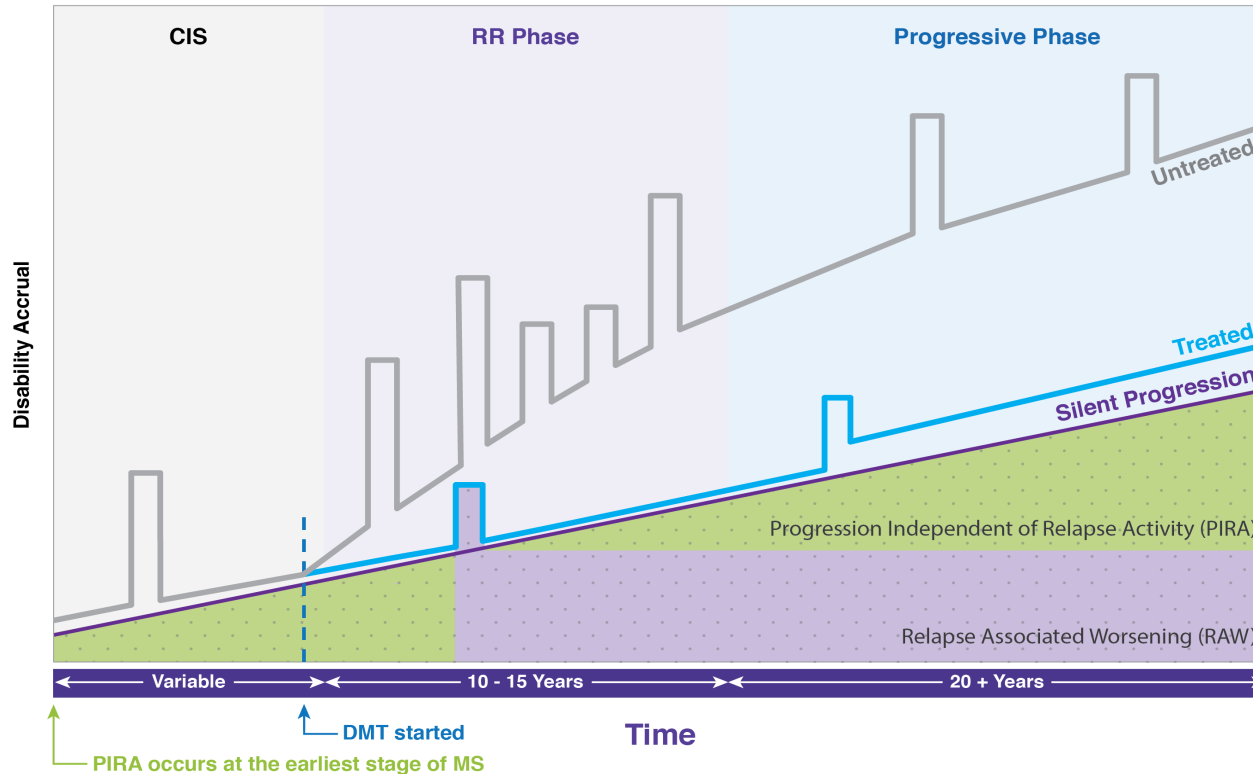
RAW is a sustained increase in disability that begins with an incomplete relapse recovery⁴.

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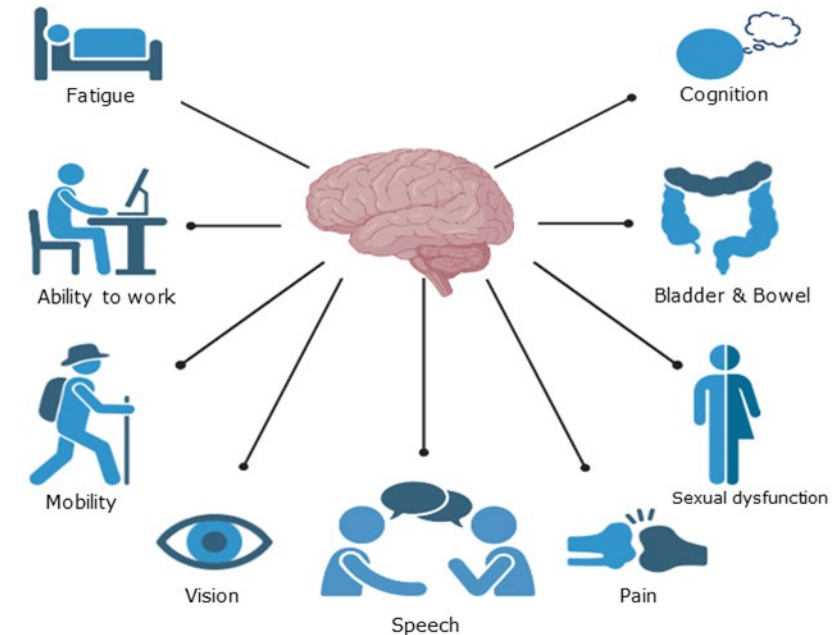
1. Giovannoni G et al. *Ther Adv Neurol Disord*. 2022;15:17562864211066751; 2. Kappos L et al. *JAMA Neurol*. 2020;77(9):1132-1140; 3. Tur C et al. *JAMA Neurol*. 2023;80(2):151-160; 4. Lublin FD et al. *Brain*. 2022;145(9):3147-3161.



Progression in MS is more than just physical disability and includes, but is not limited to, fatigue, cognitive difficulties, and balance issues¹



Patient-centric view of disease progression¹

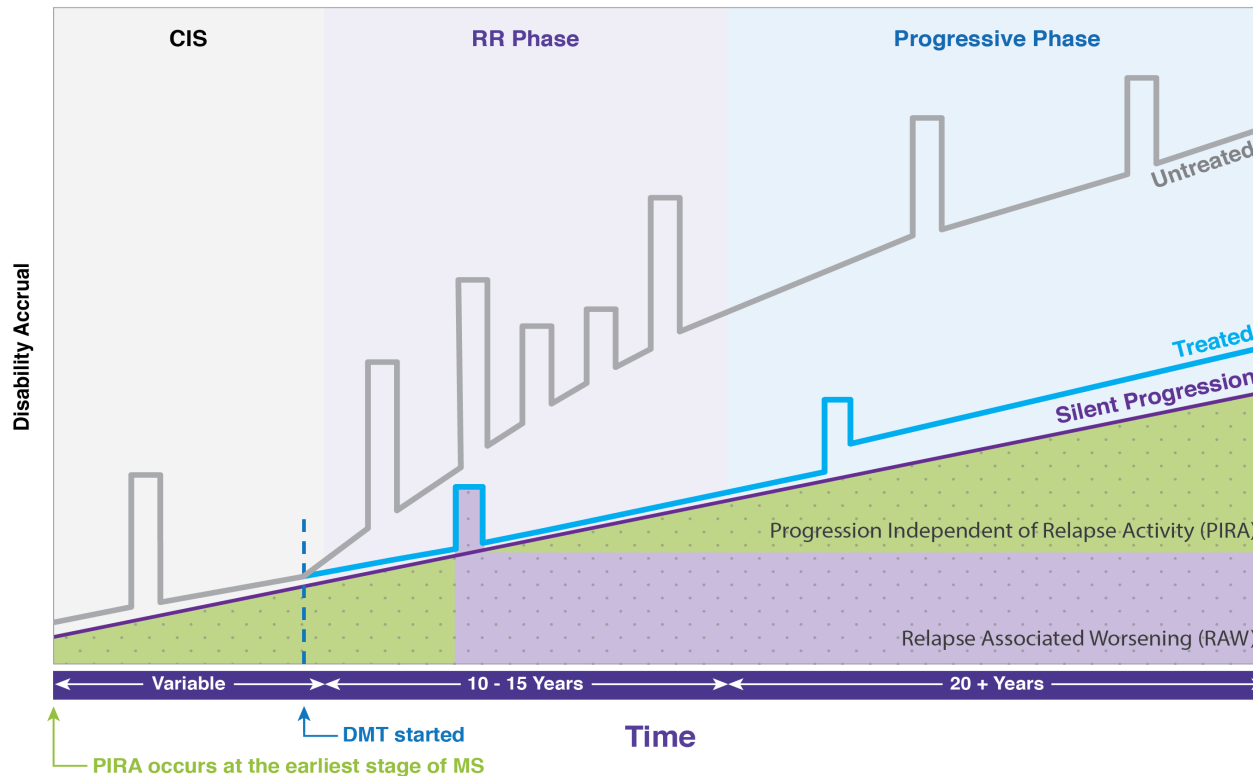


In patients with an EDSS of 0, challenge tasks unmasked deficits undetected with routine clinical tests²

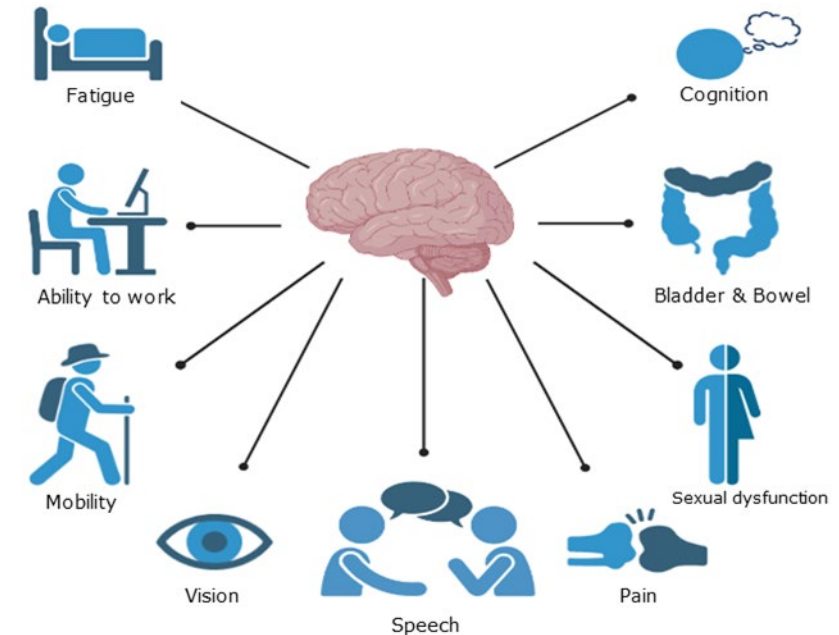
Silent progression describes the insidious disability that accrues in many patients who satisfy traditional criteria for relapsing–remitting MS³

CIS, clinically isolated syndrome; DMT, disease modifying therapy; EDSS, expanded disability status scale; MS, multiple sclerosis; PIRA; progression independent of relapse activity; RAW, relapse-associated worsening; RR, relapsing-remitting
The graphic is for illustrative purposes only and not related to the effect of specific therapies

Progression in MS is more than just physical disability and includes, but is not limited to, fatigue, cognitive difficulties, and balance issues¹



Patient-centric view of disease progression¹



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1. Marin CE et al. *Mult Scler Relat Disord*. 2021;50:102806; 2. Krieger SC et al. *Mult Scler*.2022;28(14):2299-2303; 3. University of California et al. *Ann Neurol*. 2019;85(5):653-666.



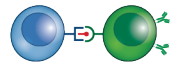
The pathologies underlying MS progression include peripherally initiated and centrally-driven processes^{1,2}

Peripherally Initiated

Adaptive Immune Cells



B cell T cell



T cell-B cell interaction

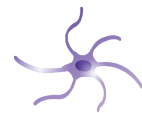
Innate Immune Cells



Macrophage



Microglia



Dendritic cell

Centrally Driven

Glia & Neurons



Astrocyte



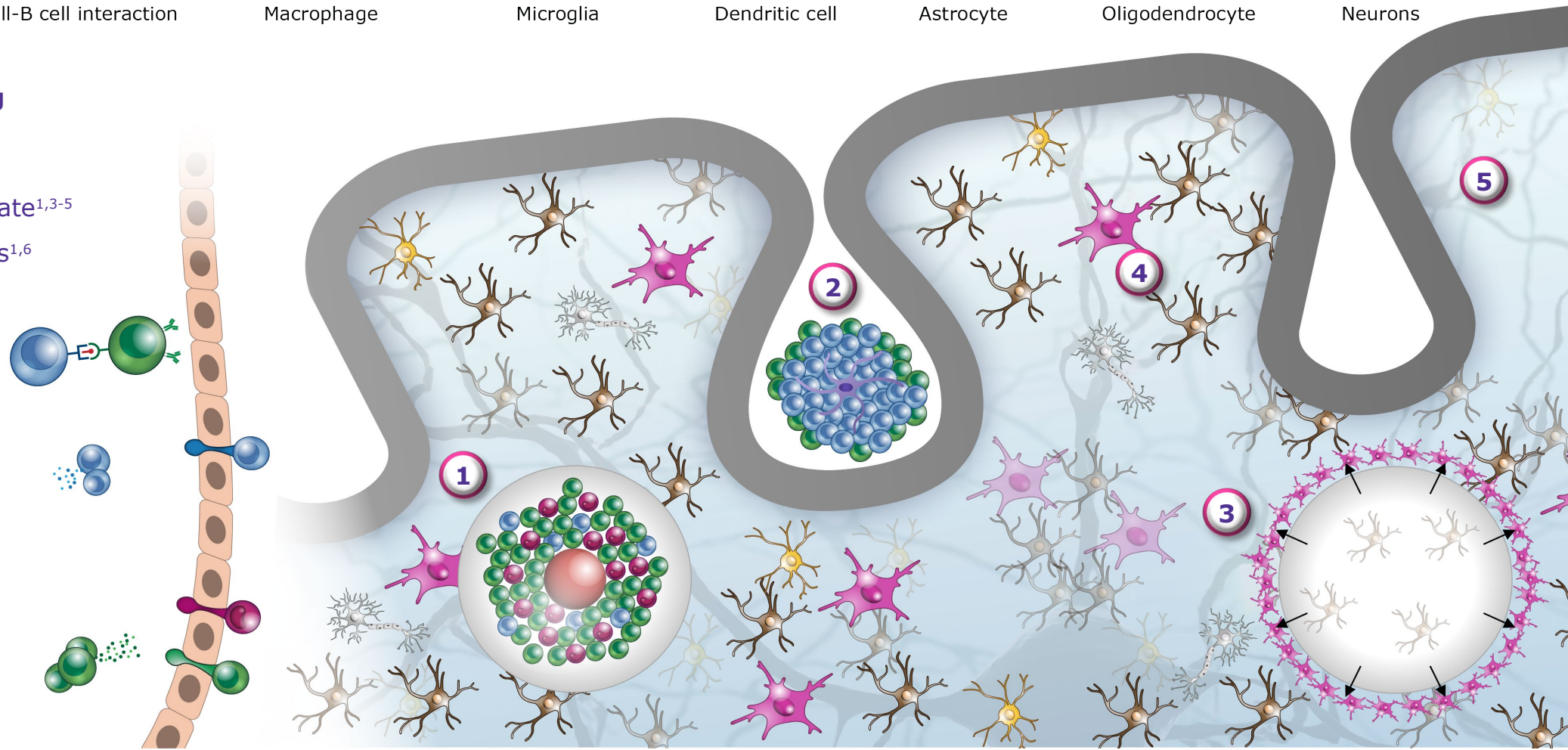
Oligodendrocyte



Neurons

Pathologies underlying MS progression¹

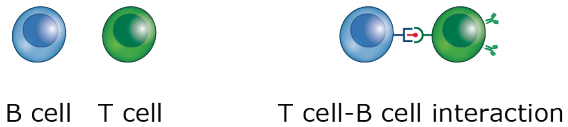
- 1 Focal MS lesions¹
- 2 Meningeal B-cell aggregate^{1,3-5}
- 3 Slowly expanding lesions^{1,6}
- 4 Diffuse gliosis^{1,7}
- 5 Age-related atrophy¹



The pathologies underlying MS progression include peripherally initiated and centrally-driven processes^{1,2}

Peripherally Initiated

Adaptive Immune Cells



Innate Immune Cells



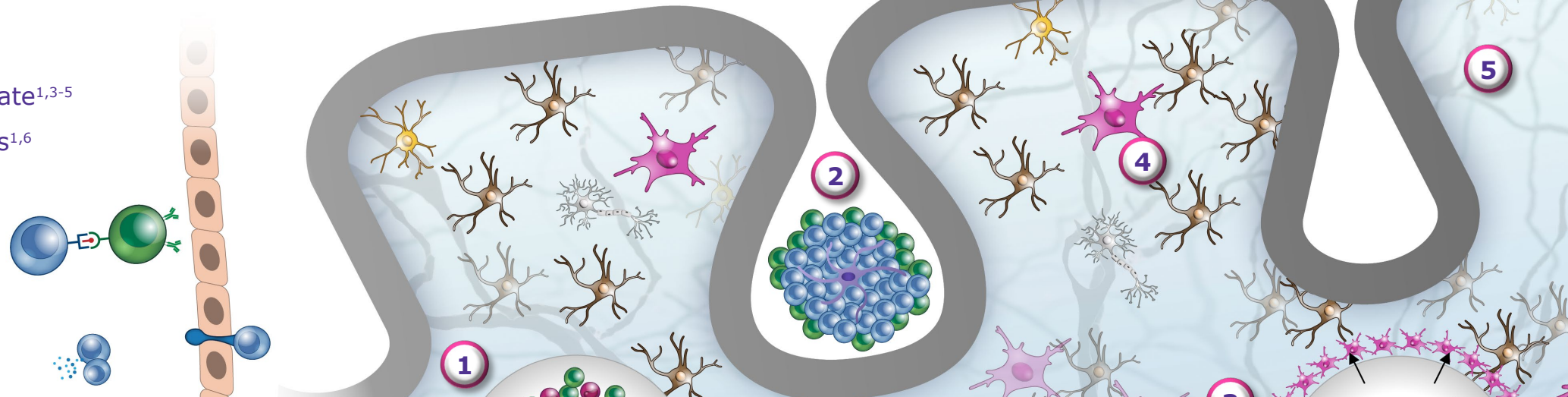
Centrally Driven

Glia & Neurons



Pathologies underlying MS progression¹

- 1 Focal MS lesions¹
- 2 Meningeal B-cell aggregate^{1,3-5}
- 3 Slowly expanding lesions^{1,6}
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- 5 Age-related atrophy¹



Peripherally initiated refers to the influx of cells from outside the CNS and Centrally-driven refers to disease processes that are compartmentalized within the CNS

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1. Hauser SL, Cree BAC. *Am J Med*. 2020;133(12):1380–1390; 2. Dendrou CA et al. *Nat Rev Immunol*. 2015;15(9):545–558; 3. Michel L et al. *Front Immunol*. 2015;6:636; 4. Serafini B et al. *Brain Pathol*. 2004;14(2):164–174; 5. Howell OW et al. *Brain*. 2011;134(9):2755–2771; 6. Elliott C et al. *Brain*. 2019;142(9):2787–2799; 7. Cavaliere C et al. *Front Cell Neurosci*. 2020;14:75.